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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,071	09/30/2005	Chuan-Yuan Li	180/156 PCT/US	6572

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JENKINS, WILSON, TAYLOR & HUNT, P. A.
SUITE 1200, UNIVERSITY TOWER
3100 TOWER BOULEVARD
DURHAM, NC 27707

EXAMINER	
LONG, SCOTT	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,071	LI ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 21* is/are pending in the application.

4a) Of the above claim(s) *17-20 and 22-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/24/2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/2005; 1/2007; 6/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner of record has changed. Please direct all further correspondence to Scott Long whose phone number is 571-272-9048.

Election/Restrictions

Examiner acknowledges the election, without traverse, of Group I directed to an adenovirus vector having an adenovirus gene under the control of a minimal promoter and a hypoxia responsive element, in the reply filed on 1 August 2007.

Claim Status

Claims 1-36 are pending. However, claims 17-20 and 22-36 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1-16 and 21 are under current examination.

Sequence Compliance

Sequence Listing and CRF have been received and are acknowledged by examiner. A statement that the Computer Readable Form (CRF) and the Sequence Listing are identical has been submitted and is acknowledged by examiner.

Oath/Declaration

The new oath or declaration, having the signatures of all inventors, received on 30 September 2005 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 24 April 2005, 16 January 2007, and 4 June 2007 consisting of 5 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit as a 371 of PCT/US03/31097 (filed 10/01/2003) which claims benefit of 60/415,319 (filed 10/01/2002). The instant application has been granted the benefit date, 1 October 2002, from the application 60/415,319.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. The embedded hyperlinks are located on page 28, line 5 and page 31, line 22. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-16 and 21 are rejected under 35 U.S.C. 102(a/e) as being anticipated by Van Meir et al. (WO02/26192, published 4/4/2002).

Claim 1 is directed to an adenovirus vector comprising an adenovirus gene under the transcriptional control of a transcriptional regulatory element (TRE) comprising a minimal promoter and a hypoxia responsive element (HRE). Van Meir et al. teach, "a recombinant virus genetically engineered to have an hypoxia-responsive element, or a multiplicity of such elements, operably linked to a promoter which is operably linked to a gene or genes which regulate or modulate replication of the virus or encode a therapeutic molecule." (page 7, lines 18-21). Van Meir et al. further describe the recombinant virus as "a recombinant replication-competent adenovirus" and "an hypoxia/HIF-dependent replicative adenovirus" (page 9, lines 10 and 13). Van Meir et al. teach, "Thus this E1A gene of an adenovirus (or any structural or functional homolog) may be engineered to be put under the control of an hypoxia responsive element/promoter, thus creating an organism that selectively replicates under hypoxic

conditions." (page 18, lines 7-10). Van Meir et al. teach an adenovirus "containing the CMV minimal promoter and the E1 gene" (page 12, line 1). See diagram of Example 4, on pages 27-28, for a more visual representation of the arrangement of elements taught by Van Meir et al. comprising HRE and minimal promoter controlling expression of E1 gene.

Claim 2 is directed to the adenovirus vector of claim 1, wherein the adenovirus gene is selected from the group consisting of an E1A gene, an E1B gene, an E2A gene, an E2B gene, and an E4 gene. Van Meir et al. teach, "Thus this E1A gene of an adenovirus (or any structural or functional homolog) may be engineered to be put under the control of an hypoxia responsive element/promoter, thus creating an organism that selectively replicates under hypoxic conditions." (page 18, lines 7-10).

Claim 3 is directed to the adenovirus vector of claim 1, further comprising a second adenovirus gene under the transcriptional control of the TRE. Van Meir et al. teach, "recombinant adenoviruses were able to express constitutively (Ad-CMV-E1) or conditionally (HYPR-Ad1) E1A and E1B gene products. " (page 34, lines 1-2). See also Figure 6.

Claim 4 is directed to the adenovirus vector of claim 1, wherein the minimal promoter is selected from the group consisting of the cytomegalovirus (CMV) minimal promoter, the human β-actin minimal promoter, the human EF2 minimal promoter, and the adenovirus E1B minimal promoter. Van Meir et al. teach an adenovirus "containing the CMV minimal promoter and the E1 gene" (page 12, line 1).

Claim 5 is directed to the adenovirus vector of claim 4, wherein the CMV minimal promoter comprises SEQ ID NO: 1. Van Meir et al. teach an adenovirus "containing the CMV minimal promoter" (page 12, line 1).

Claim 6 is directed to the adenovirus vector of claim 1, wherein the HRE is derived from the human vascular endothelial growth factor (VEGF) promoter. Van Meir et al. teach, "based on this information, EPO and VEGF HRE's were chosen for the design and testing of a hypoxia-responsive promoter" (page 19, lines 1-2).

Claim 7 is directed to the adenovirus vector of claim 6, wherein the HRE comprises SEQ ID NO: 2. Van Meir et al. teach "the VEGF [HRE] sequence... CCACAGTGC TACGTGGGCT CCUCAGGTC CTCTT" which is 100% identical to SEQ ID NO:2 of the instant application.

Claim 8 is directed to the adenovirus vector of claim 7, wherein the HRE comprises five tandem copies of SEQ ID NO: 2. See Van Meir et al., Figure 2, where up to 6 tandem copies of HRE are shown and page 10-11 for detailed description of figure.

Claim 9 is directed to the adenovirus vector of claim 1, further comprising a transgene. Van Meir et al. teach that their adenoviruses express anti-angiogenic factors (page 13, lines 23-26, and page 15, lines 10-15).

Claim 10 is directed to the adenovirus vector of claim 9, wherein the transgene is a second adenovirus gene. Van Meir et al. teach, "recombinant adenoviruses were able to express constitutively (Ad-CMV-E1) or conditionally (HYPR-Ad1) E1A and E1B gene products. " (page 34, lines 1-2).

Claim 11 is directed to the adenovirus vector of claim 9, wherein the transgene encodes an immunostimulatory molecule. Meir et al. teach "genes which can be used in the invention include...IL-12" (page 23, lines 8-14).

Claim 12 is directed to the adenovirus vector of claim 11, wherein the immunostimulatory molecule is selected from the group consisting of IL2 and IL12. Van Meir et al. teach "genes which can be used in the invention include...IL-12" (page 23, lines 8-14).

Claim 13 is directed to the adenovirus vector of claim 9, wherein the transgene is a suicide gene. Van Meir et al. teach, "Recombinant viruses of the invention can be further engineered to contain a gene that allows for the termination of viral propagation with an exogenous agent, such as thymidine kinase, which would render them susceptible to ganciclovir." (page 19, lines 28-29 through page 20, line 1).

Claim 14 is directed to the adenovirus vector of claim 13, wherein the suicide gene is selected from the group consisting of a TNF-α gene, a Trail gene, a Bax gene, an HSV-tk gene, a cytosine deaminase gene, a p450 gene, and a diphtheria toxin gene, an s-Flt1 gene, and an ex-Flk1 gene. Van Meir et al. teach, "Recombinant viruses of the invention can be further engineered to contain a gene that allows for the termination of viral propagation with an exogenous agent, such as thymidine kinase, which would render them susceptible to ganciclovir." (page 19, lines 28-29 through page 20, line 1).

Claim 15 is directed to a composition comprising the adenovirus vector of claim 1. Van Meir et al. teach, "compositions of the invention comprise a recombinant virus genetically engineered to have an hypoxia-responsive element, or a multiplicity of such

elements, operably linked to a promoter which is operably linked to a gene or genes which regulate or modulate replication of the virus or encode a therapeutic molecule." (page 7, lines 18-21).

Claim 16 is directed to the composition of claim 15, further comprising a pharmaceutically acceptable carrier. Inherently, any aqueous solution of the adenoviral composition of claim 15 would be a pharmaceutically acceptable carrier.

Claim 21 is directed to a host cell comprising the adenovirus vector of claim 1. Van Meir et al. teach, "expression of recombinant viral gene products in transfected cells under hypoxic and normoxic conditions.... adenoviruses, U251MG and LN-229 cells were infected with the Ad-CMV-E1 and HYPR-Ad1" (page 33, lines 17-29).

Accordingly, Van Meir et al. anticipated the instant claims.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott Long
Patent Examiner
Art Unit 1633

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE